Inductive Control of a Ring–Chain Tautomeric Equilibrium

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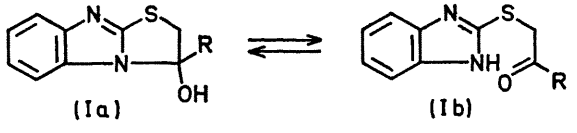
Summary 3-Hydroxy-3-trifluoromethyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazole exists only as the cyclic carbinolamine in the solid state and in solution while the corresponding 3-hydroxy-3-t-butyl derivative exists solely as the open-chain amino-ketone tautomer.

RING–CHAIN tautomerism has been observed in several compounds.[1] A number of reports have appeared concerning the influence of inductive and resonance effects of substituted aromatics on the position of the tautomeric equilibrium.[2–6] Dorman[7] has shown that on increasing the size of the 2-alkyl group in 2-alkyl-4,5-dimethyl-6-phenyltetrahydro-2*H*-1,3,4-oxadiazines from methyl to t-butyl the tautomeric equilibrium is shifted towards the chain γ-hydroxy-hydrazone tautomer. I report the first evidence for the control of a ring–chain tautomeric equilibrium solely by the inductive effect of simple aliphatic substituents.

I.r. and n.m.r. measurements have shown that 3-hydroxy-2,3-dihydrothiazolo[3,2-*a*]benzimidazole exists only as the cyclic carbinolamine (Ia; R = H) in the solid state or in solution.[8] The 3-methyl derivative (I; R = Me) also exists as (Ia) in the solid state but in solution is a 1 : 2 mixture of (Ia) and the open-chain amino-ketone (Ib), respectively. In agreement with Dorman,[7] I have found



(Ia) (Ib)

that increasing the size of R to t-butyl shifts the equilibrium towards the chain tautomer. Treatment of 1-bromo-3,3-dimethylbutan-2-one with benzimidazoline-2-thione in butan-2-one gave (I; R = Bu^t) m.p. 104·5—105·5°, in 70% yield.† This compound exists only as the open-chain tautomer (Ib) both in the solid state and in solution. The i.r. spectrum of the compound as a KBr disc showed broad absorption bands at 3100—2600 (NH stretching) and a sharp, intense band at 1712 cm^{-1} (CO stretching). In chloroform solution, the carbonyl absorption appeared at 1705 cm^{-1} and NH stretching vibrations were observed at

† *Satisfactory elemental analyses were obtained for all new compounds.*

3455 (free NH) and 3307 (bonded NH) cm^{-1}. There were no absorption bands which could be attributed to C–O stretching of a tertiary alcohol (1040—1200 cm^{-1}). The n.m.r. spectrum of (I; R = Bu^t) ($CDCl_3$ with $SiMe_4$ as internal standard) showed a singlet at 1·12 [9H, $(CH_3)_3C$] and a singlet at 4·45 p.p.m. (2H, CH_2). In $(CD_3)_2SO$ the corresponding bands appeared at 1·20 and 4·62 p.p.m., respectively. In either solvent, no quartet was observed for the methylene protons as was reported for (Ia; R = Me)[8] and expected for (Ia; R = Bu^t).

Treatment of 1-bromo-3,3,3-trifluoropropan-2-one with benzimidazoline-2-thione in butan-2-one gave (I; R = CF_3), m.p. 138·0—139·0°, in 61% yield.† Both i.r. and n.m.r. spectra clearly indicated that the trifluoromethyl compound exists only as the ring tautomer(Ia). The solid-state i.r. spectrum (KBr disc) showed a broad band for OH stretching in the region of 3100—2550 and C–O stretching for a tertiary alcohol at 1182 cm^{-1}. In chloroform solution, the corresponding bands appeared at 3100—2600 and 1188 cm^{-1}, respectively. Both spectra showed no evidence of carbonyl stretching (1650—1800 cm^{-1}). The n.m.r. spectrum [$(CD_3)_2SO$] exhibited three absorptions at 4·31, 7·12—7·75, and 9·00 p.p.m. in the ratio 2·0 : 4·0 : 1·0. The high-field signal appeared as an AB quartet (J_{AB} 18 Hz) and is assigned to the methylene protons of (Ia; R = CF_3). The hydroxyl proton appeared at lowest field and disappeared after exchange with deuterium oxide. The multiplet at 7·12—7·75 p.p.m. is assigned to the four aromatic protons.

Consideration of steric effects alone suggests that the proportion of chain tautomer for (I; R = CF_3), would be between that observed for the methyl and t-butyl derivatives.[9] However, no evidence was obtained for the presence of any oxo-form (Ib; R = CF_3). The trifluoromethyl group is strongly electron withdrawing thus rendering the carbonyl carbon more positive and hence more susceptible to ring formation with the amino-group. Consequently, the major tautomer would be (Ia; R = CF_3). The complete absence of (Ib; R = CF_3) illustrates the importance of inductive effects on the ring–chain tautomeric equilibrium for simple aliphatic substituents.

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